Psychological distress and chronic obstructive pulmonary disease in the Renfrew and Paisley (MIDSPAN) study

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RESEARCH REPORT

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Background: This study examined whether psychological distress might be a predictor of chronic obstructive pulmonary disease (COPD).

Method: The relation between psychological distress at baseline, measured by the general health questionnaire (GHQ), and chronic bronchitis three years later, as measured by the Medical Research Council (MRC) bronchitis questionnaire and forced expiratory flow in one second (FEV_1), was examined in 1682 men and 2203 women from the Renfrew and Paisley (MIDSPAN) study. The analyses were run on men and women separately and adjustments were made for age, socioeconomic position, and lung function at baseline (FEV_1). People with chronic diseases at baseline were then excluded to give a ''healthy'' baseline cohort. The effect of psychological distress on individual components of the MRC bronchitis questionnaire and FEV_1 was also assessed.

Results: In multivariate analyses of the whole cohort baseline psychological distress in women was associated with reduced FEV_1 at follow up (OR 1.31 95% CI 1.0 to 1.73) after adjustment. In women, in the healthy cohort, psychological distress was associated with chronic bronchitis (OR 2.00, 95% CI 1.16 to 3.46), symptoms of bronchial infection (OR 2.14, 95% CI 1.44 to 3.19), symptoms of breathlessness (OR 3.02, 95% CI 1.99 to 4.59), and reduced FEV_1 (OR 1.62, 95% CI 1.13 to 2.32). In men psychological distress predicted symptoms of bronchial infection (OR 2.09, 95% CI 1.28 to 3.42).

Conclusion: This study supports research suggesting that psychological distress is associated with COPD and shows that psychological distress predicts COPD in women. The robustness of the association and the exact mechanism requires further investigation.

The coexistence of psychological distress and chronic organic disease is of great clinical importance as it adversely affects the patient's quality of life and may lead to a downward spiral in health. Psychological distress may reduce the person's ability to cope with physical symptoms, which may lead to further debility and worsening of the psychological distress.[1 2] The situation may be complicated further if symptoms are attributed to the organic disease and not recognised as attributable to psychological distress.

A recent literature review found an increased prevalence of anxiety disorders in chronic obstructive pulmonary disease (COPD) sufferers.[3] COPD has been reported to coexist with a higher prevalence of depression.[4 5] A more stringent systematic review of COPD and depression was inconclusive: two studies that were methodologically well conducted did not find an association, however they lacked power, while larger studies found an increased prevalence of depression.[1] New therapeutic approaches might be developed through better understanding of the association between psychological distress and COPD.

This investigation is a secondary analysis using data from the Renfrew and Paisley (MIDSPAN) study to investigate the association between psychological distress at baseline and COPD a few years later.

METHOD

The Renfrew and Paisley (MIDSPAN) study was a longitudinal study of 15 411 adults aged 45 and 64 years old from two towns near Glasgow. The respondents were asked to complete a questionnaire and attend a clinic for screening examinations between 1972 and 1976.[6] Appropriate local research ethics committees approved the study protocol. Overall there was an 80% response rate. Participants were invited for a follow up visit between 1977 and 1979. The median time between baseline and follow up was 3 years 5 months (interquartile range 1 year 9 months). Psychological distress was only measured in the Paisley cohort seven months after the start of the survey in September 1974. This meant that 3782 men and 4680 women completed the questionnaire. Those that completed this questionnaire were more likely to be manual class (60%) and married (78%). Analyses were carried out only on those respondents with values on all variables used in the database. A ''healthy'' baseline cohort was also created of those who did not have a history of symptoms of angina, ECG ischaemia, diabetes, stroke, or bronchitis at baseline (1098 men and 1555 women). This was to reduce confounding from comorbidity and the effect of negative affectivity by also excluding those who may be demonstrating a tendency to symptom reporting.[7–10] Men and women were analysed separately because a smaller number of men are affected by psychological distress but men have a higher prevalence of chronic bronchitis and are more likely to smoke.[11] This may make it more difficult to statistically find a subtle association in men.

Outcome measures

A self report questionnaire gathered socioeconomic data and history of symptoms of certain chronic diseases at baseline and follow up. The outcomes measures used in this study were those that were recorded at follow up. The Medical Research Council (MRC) bronchitis questionnaire was included in the survey.[12] This identifies sufferers of COPD based on their symptoms.[13] This questionnaire has been

Abbreviations: COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory flow in one second; MRC, Medical Research Council

adapted to define the subject as having chronic bronchitis if they answered ''yes'' to all of the following questions[14]:

Chronic sputum
''Do you usually bring up any phlegm from your chest first thing in the morning in the winter?'' and ''Do you bring up phlegm like this for as much as three months in the winter each year?''

Breathlessness
''Do you get short of breath walking with people of your own age on level ground?''

A screening examination recorded height, weight, and forced expiratory volume in one second (FEV_1) and an ECG was taken. FEV_1 was measured with a vitalograph spirometer while standing: after a practice blow the higher of two attempts was recorded.[15] These measurements were converted to a FEV_1 score, which was a percentage of the predicted FEV_1. Predicted FEV_1 was constructed from linear regression of age, height, and sex of those in the survey who had never smoked and did not report respiratory symptoms.[15] A score of 75 was our criterion for pulmonary obstruction.[1]

The breathlessness criteria for chronic bronchitis were used as the primary outcomes in the healthy cohort. Those who answered ''yes'' to the MRC question; ''In the past three years have you had a period of increased cough and phlegm lasting three weeks or more?'' were added to those reporting chronic sputum and called the ''phlegm'' group. This gave our criterion for chronic or recurrent bronchitis.[12]

Predictor
The 30 item general health questionnaire (GHQ-30) detects psychological distress by identifying problems in carrying out ''healthy'' functions and the emergence of distressing problems.[16] Participants who responded positively to four or more questions were considered to have psychological distress. This threshold for psychological distress was independently validated on 166 subjects, drawn from this cohort and eight English settings, finding a sensitivity of 72.0% and a specificity of 88.5% for psychological distress.[17]

Analyses
The statistical analyses were carried out with SPSS (Statistical Package for the Social Sciences) for Windows (version 10.0). Baseline characteristics of GHQ positive and negative respondents were compared using χ^2, *t* test, and analysis of variance. The association between psychological distress and various indicators of COPD at follow up was assessed using logistic regression in men and women separately. The first model in the healthy cohort adjusted for age, social class (non-manual I-IIIN or manual class IIIM-V),[18] and marital status (married or not married, including divorced and widowed). In the subsequent analysis FEV_1 and tertiles of body mass index were also adjusted for. These analyses were repeated on the sample from the cohort who reported never having smoked.

RESULTS
Table 1 shows the relations between psychological distress and baseline characteristics. At baseline 14% (405 of 2931) of men and 20% (718 of 3644) of women were considered to have psychological distress. Some 18.2% (533 of 2931) of men and 9.6% (350/3644) of women had chronic bronchitis as defined by the MRC bronchitis questionnaire and no association was found with psychological distress. The mean FEV_1 score was significantly lower in men and women with psychological distress.

Women with psychological distress were on average one year younger and smoked more than their non-distressed counterparts. Men with psychological distress also smoked more than men without psychological distress. Manual social classes had a higher level of psychological distress among

Table 1 Cohort baseline characteristics of GHQ negative and positive men and women

	GHQ negative men n (%)	GHQ positive men n (%)	GHQ negative women n (%)	GHQ positive women n (%)
Number	2526 (86.0)	405 (14.0)	2926 (80.0)	718 (20.0)**
Chronic bronchitis	448 (17.7)	65 (16.0)	271 (9.3)	79 (11.0)
No chronic bronchitis	2078 (82.3)	340 (84.0)	2655 (90.7)	639 (89.0)
Mean age (SD)	54 (5.6)	54 (5.6)	55 (5.5)	54 (5.5)**
Smoking habits:				
Never	441 (17.5)	56 (13.8)*	1393 (47.6)	282 (39.3)**
Smoker	1412 (55.9)	262 (64.7)*	1298 (44.4)	385 (53.6)**
Former smoker	673 (26.6)	87 (21.5)	235 (8.0)	51 (7.1)
Social class:				
Non-manual	901 (35.7)	124 (30.6)*	1414 (48.3)	316 (44.0)*
Manual	1625 (64.3)	281 (69.4)	1512 (51.7)	402 (56.0)
Marital status:				
Married	2232 (88.4)	332 (82.0)**	2078 (71.0)	513 (71.4)
Not married	294 (11.6)	73 (18.0)	848 (29.0)	205 (28.6)
Mean BMI (SD)	26.0 (3.4)	25.6 (3.4)*	25.5 (4.2)	25.3 (4.6)**
Angina				
Yes	362 (14.3)	262 (64.7)**	340 (11.6)	207 (28.8)**
No	2164 (85.7)	143 (35.3)	2586 (88.4)	511 (71.2)
Mean FEV_1 score (SD)	89.6 (22.3)	84.9 (24.6)**	93.1 (22.9)	88.0 (24.0)**
Phlegm:				
Yes	823 (32.6)	194 (47.9)**	547 (18.7)	212 (29.5)**
No	1703 (67.4)	211 (52.1)	2379 (81.3)	506 (70.5)
Breathlessness:				
Yes	251 (10.0)	120 (29.6)**	313 (10.7)	219 (30.6)**
No	2267 (90.0)	285 (70.4)	2605 (89.3)	496 (69.4)
Stroke:				
Yes	26 (1.0)	11 (2.7)*	18 (0.6)	15 (2.1)**
No	2500 (99.0)	394 (97.3)	2908 (99.4)	3611 (99.1)
Diabetes:				
Yes	39 (1.5)	4 (1.0)	27 (0.9)	10 (1.4)
No	2487 (98.5)	401 (99.0)	2899 (99.1)	708 (98.6)

*p<0.05; **p<0.001.

Table 2 Odds ratio of different measures of respiratory disorder in ''healthy'' men and women at follow up by GHQ status at baseline

	New cases at follow up	OR*	95% CI	OR†	95% CI
Men					
MRC chronic bronchitis	295	1.51	0.83 to 2.73	1.49	0.83 to 2.71
MRC phlegm	519	2.15	1.33 to 3.48	2.09	1.28 to 3.42
MRC breathlessness	230	1.43	0.68 to 3.02	1.40	0.65 to 3.00
FEV_1 ⩽75%	409	0.86	0.49 to 1.50	0.86	0.49 to 1.49
Women					
MRC chronic bronchitis	191	2.08	1.21 to 3.57	2.00	1.16 to 3.46
Never smokers	73	2.56	1.05 to 6.25	2.53	0.99 to 6.43
MRC phlegm	410	2.25	1.52 to 3.32	2.14	1.44 to 3.19
Never smokers	133	2.00	0.96 to 4.17	2.01	0.93 to 4.31
MRC breathlessness	327	2.90	1.94 to 4.33	3.02	1.99 to 4.59
Never smokers	144	2.73	1.41 to 5.27	3.23	1.62 to 6.47
FEV_1 ⩽75%	419	1.60	1.12 to 2.29	1.62	1.13 to 2.32
Never smokers	177	1.13	0.62 to 2.05	1.14	0.62 to 2.08

*Adjusted for baseline age, and socioeconomic factors. †Adjusted for baseline age, socioeconomic factors, BMI, and FEV_1.

both men and women. Men with psychological distress were less likely to be married than men without psychological distress. Lower body mass index and angina pectoris were both associated with a higher prevalence of psychological distress in women and more strongly in men. A higher percentage of men and women with a history of stroke had psychological distress. There was no significant association between diabetes and psychological distress.

The relations between psychological distress and these characteristics were analysed in the cohort of 1682 men and 2203 women who returned for follow up. The association between baseline smoking, social class and bronchitis at follow up in men was (OR = 1.77 95%CI 1.21 to 2.59), (OR = 1.30 95% CI 1.00 to 1.69) respectively, and in women was (OR = 1.89 95% CI 1.38 to 2.57), (OR = 1.24 95% CI 0.92 to 1.67).

In the whole healthy cohort baseline psychological distress was associated with an almost twofold increased risk of reporting MRC phlegm at follow up in fully adjusted analysis (OR 1.73 95% CI 1.43 to 2.10). Psychological distress was more weakly associated with MRC chronic bronchitis and breathlessness (table 2). Baseline psychological distress was also associated with a twofold increased risk of chronic bronchitis in women, rising to 2.5 times the risk in never smokers. Furthermore, psychological distress was associated with over twice the risk of reporting MRC phlegm and over three times the risk of reporting breathlessness at follow up in women in fully adjusted analysis (table 2). Psychological distress was also associated with increased risk of FEV_1 ⩽75%, which was maintained after adjustment but was not present in never smokers.

DISCUSSION

Psychological distress at baseline was associated with angina, stroke, reduced FEV_1, symptoms of breathlessness, and infective bronchitis but not chronic bronchitis. Women with psychological distress at baseline had increased risk of developing chronic bronchitis, bronchial infection, breathlessness, and reduced FEV_1 at follow up in multivariate analyses. In the women who never smoked there was an association between baseline psychological distress and developing chronic bronchitis and breathlessness but not phlegm nor reduced FEV_1. In men psychological distress was associated with symptoms of bronchial infection at follow up.

Methodological issues

The sample used in this study may confer some selection bias. Although roughly 80% of the targeted population responded, the cohort used in this study is considerably smaller because those who did not complete all sections of the survey were excluded. However, a sizeable community cohort of men and women remains and there is no obvious reason why the association between psychological distress and COPD should be affected.

Residual confounding is a potential problem with this study.[10] It has been argued that psychological distress is caused by material and social inequalities and is a symptom of deprivation.[10] However, the GHQ has been found to identify people with real psychological distress with high standards of reliability and validity[16 17] and was commonly used at the time of the study. Moreover, the risk of bronchitis associated with socioeconomic status is lower than the risk associated with psychological distress and does not support the contention that psychological distress is merely a proxy measure of social deprivation.

Sex differences

Throughout the analyses, with the exception of phlegm, women showed more robust associations than men. COPD in women is a comparatively underinvestigated area and fossil fuel pollution has been found to have a greater effect in

Key messages

- Women with psychological distress were found to have an odds ratio of 1.5 for chronic bronchitis at follow up several years later
- Psychological distress in women predicted objective as well as subjective parameters of lung function suggesting that results cannot be entirely explained by symptom reporting.

Policy implications

- Amelioration of women's psychological distress in deprived populations could prevent future physical ill health.
- There is a need for recognition of psychological factors in the aetiology and management of COPD.

women compared with men.[19] However, formal interaction tests did not conclusively find that sex had an effect on the relation between psychological distress and chronic bronchitis ($p = 0.86$).

Causality

Psychological distress could cause increased reporting of COPD through sufferers overstating minor symptoms[7] and reporting breathlessness that results from their psychological distress.[20] However, this is unlikely to explain the association between psychological distress and reduced FEV_1. Psychological distress can confer a greater indirect risk profile for COPD through smoking[21–24] and apathy that could cause lower levels of self care and lower activity levels.[9] The similarity in magnitude of the associations between psychological distress and the self report outcomes of MRC chronic bronchitis, phlegm, and breathlessness in never smokers do not support a pathway between psychological distress and chronic bronchitis mediated through health behaviours, of which smoking would perforce be the most influential. But the lack of association between psychological distress and the ''objective outcome'' of reduced FEV_1 in non-smokers must place some doubt on causal mechanisms that exclude smoking as an explanatory factor.

It has been suggested that depression affects the autonomic nervous system, particularly the hypothalamic-pituitary-adrenal (HPA) pathway.[25 26] This could increase cortisol release with immunosuppressive results.[25] This could increase the risk of developing infections, which could contribute to COPD. Bronchial dilatation and reduced organ blood flow could result from up-regulation in the sympathetic neurons or a down-regulation in the parasympathetic pathways, or both.[8]

Barbiturates and benzodiazepines were both widely used treatments for psychological distress and may produce symptoms of breathlessness,[27] whereas treatment of psychological distress could reduce its ''toxic'' effect. Unfortunately, the treatment regimens of those with psychological distress were not recorded in this cohort.

Although the mechanism of these associations is unclear there are some potential implications for the prevention of chronic bronchitis. It is possible that psychological distress in deprived populations may have more consequences for subsequent physical health than in less deprived populations. Recognition and management of psychological distress, especially in women, as seen in this cohort, may lead to healthier behaviours, more physical activity, less smoking, and better future physical health.

Conclusion

This study supports previous work that has shown that psychological distress is associated with COPD[1–5] and, further suggests that psychological distress predicts COPD in women. In this study women with psychological distress were found to be roughly 1.5 times more likely to develop symptoms of COPD and have reduced recordings of FEV_1 several years later at follow up. The question remains whether treating psychological distress can prevent the increase in COPD.

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